EIF2AK4 gene

eukaryotic translation initiation factor 2 alpha kinase 4

Normal Function

The *EIF2AK4* gene provides instructions for making a protein that helps direct a cell's response to changes that could damage the cell. This protein is found in several tissues throughout the body, including blood vessel walls. The EIF2AK4 protein can turn on (activate) another protein called eIF2 alpha (eIF2α), which helps control protein production. When cells are under stress, for example when the level of protein building blocks (amino acids) is too low, EIF2AK4 activates eIF2α. When turned on, eIF2α stimulates processes that reduce protein production, which helps conserve amino acids. In addition, activated eIF2α can trigger production of certain proteins called transcription factors, which control gene activity. The transcription factors regulated by eIF2α control the activity of genes involved in processes that help reduce the stress on the cell.

Health Conditions Related to Genetic Changes

pulmonary arterial hypertension

pulmonary veno-occlusive disease

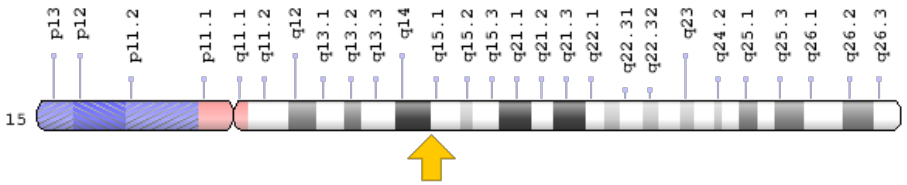
Mutations in the *EIF2AK4* gene are the primary genetic cause of a condition called pulmonary veno-occlusive disease (PVOD); at least 22 mutations in this gene have been found in affected individuals. In PVOD, excess fibrous tissue builds up in the small vessels in the lungs that carry oxygenated blood from the lungs to the heart (the pulmonary veins). This buildup narrows (occludes) the vessels and impairs blood flow. Because blood flow through the lungs is difficult, pressure rises in the vessels that carry blood that needs to be oxygenated to the lungs from the heart (pulmonary arteries). Increased pressure in these vessels is known as pulmonary arterial hypertension.

The *EIF2AK4* gene mutations involved in PVOD likely lead to a complete loss of functional protein. It is not known how absence of EIF2AK4 protein function leads to the pulmonary vein abnormalities characteristic of PVOD.

Chromosomal Location

Cytogenetic Location: 15q15.1, which is the long (q) arm of chromosome 15 at position 15.1

Molecular Location: base pairs 39,934,101 to 40,035,596 on chromosome 15 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- E2AK4_HUMAN
- eukaryotic translation initiation factor 2-alpha kinase 4
- GCN2
- GCN2 eIF2alpha kinase
- GCN2-like protein
- general control nonderepressible 2
- KIAA1338
- PVOD2

Additional Information & Resources

Educational Resources

- Madame Curie Biosciences Database (2000): Mechanism of Translation Initiation in Eukaryotes
  https://www.ncbi.nlm.nih.gov/books/NBK6597/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28EIF2AK4%5BTIAB%5D%29+OR+%28eukaryotic+translation+initiation+factor+2+alpha+kinase+4%5BTIAB%5D%29%29+OR+%28%28GCN2+eIF2alpha+kinase%5BTIAB%5D%29+OR+%28GCN2%5BTIAB%5D%29+OR+%28eukaryotic+translation+initiation+factor+2-alpha+kinase+4%5BTIAB%5D%29+OR+%28general+control+nonderepressible+2%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- EUKARYOTIC TRANSLATION INITIATION FACTOR 2-ALPHA KINASE 4
  http://omim.org/entry/609280

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_EIF2AK4.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=EIF2AK4%5Bgene%5D
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=19687
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/440275
- UniProt
  http://www.uniprot.org/uniprot/Q9P2K8

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